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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,247	02/14/2002	Paul A. Wender	8400-0013	3262

23980 7590 03/15/2006

REED INTELLECTUAL PROPERTY LAW GROUP
1400 PAGE MILL ROAD
PALO ALTO, CA 94304-1124

EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,247	WENDER ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/15/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *3-6,9-16 and 20-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7,8,17-19 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/24/03, 7/15/04, 8/22/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group II invention, election of a transport moiety and a conjugate species in the reply filed on December 15, 2005 is acknowledged. Amendments to claims and specifications filed are also acknowledged. The traversal is on the ground(s) that Examiner found inventions I-IV and V related by process of making and process of using in the election/restrictions. This is not found persuasive because the process of making the product results in product.

The requirement is still deemed proper and is therefore made FINAL.

Examiner searched the elected transport moiety species is the structure (R aca)$_6$R wherein R is arginine, aca is ϵ-amino caproic acid and found to be free of art and hence constitute allowable subject matter. Examiner extended the search and found art on RKRKR where R is arginine and K is lysine.

Claims 3-6, 9-16 and 20-29 are withdrawn from further consideration as being drawn to non elected species.

Claims 30-35 are withdrawn from further consideration as being drawn to non elected invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7 and 8 rejected under 35 U.S.C. 102(b) as being anticipated by Lorenzen, et al., The Journal of Cell Biology, 1995, 131, 631-643.

In the instant application, applicants claim a composition comprising a biologically active compound and a transport moiety comprising a structure $(ZY)_nZ$ wherein Z is L-arginine or D-arginine and Y is independently an amino acid that does not comprise an amidino or guanidine moiety and 'n' is an integer from 2 to 10.

Lorenzen, et al., teaches splicing of non-catalytic domain of human T-cell protein tyrosine phosphatase to generate 45-kD ($p45^{TC}$) and 48-kD ($p48^{TC}$) segments targeting the two forms to two different subcellular compartments. The $p45^{TC}$ segment localizes in the nucleus the sequence RKRKR that precedes the splice junction function acts as a nuclear localization signal (abstract). The splicing of the segment comprising the nuclear localization signal (RKRKR) (wherein R is arginine and K is lysine) with the tyrosine phosphatase enzyme as the biologically active molecule meets the limitations of claims 1 and 2. In the absence of a proper definition for a 'linking moiety' in the claims, splicing of the two segments meets the limitations of claim 7.

Claim Rejections - 35 USC § 103

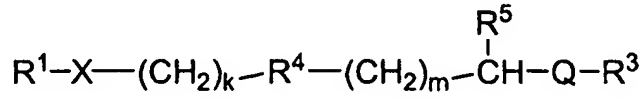
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 7, 8, 17-19 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lorenzen, et al., The Journal of Cell Biology, 1995, 131, 631-643, in view of US 4,409,141 issued to Noda, et al.

In the instant application, applicants claim a composition comprising a biologically active compound and a transport moiety comprising a structure $(ZY)_nZ$ wherein Z is L-arginine or D-arginine and Y is independently an amino acid that does not comprise an amidino or guanidine moiety and 'n' is an integer from 2 to 10. Applicants also claim a linking moiety to form a conjugate of the following formula,



wherein X is -OC(O)-, Q is -NHC(O)-, k is 1, m is 1, R^4 is S, and R^5 is $-C(O)NH_2$
R1 is biologically active compound and R3 is the transport moiety.

Lorenzen, et al., teaches splicing of non-catalytic domain of human T-cell protein tyrosine phosphatase to generate 45-kD ($p45^{TC}$) and 48-kD ($p48^{TC}$) segments targeting the two forms to two different subcellular compartments. The $p45^{TC}$ segment localizes in the nucleus the

sequence RKRKR that precedes the splice junction function acts as a nuclear localization signal (abstract). The nuclear localization signal, which constitutes the transport moiety directing the transport into the nucleus is characterized by high proportions of basic amino acid residues and it requires 3 out of 5 amino acids, be basic at the C-terminal end. The reference also mentions that the right and left elements of the NLS be separated by a spacer typically of 10 or 11 amino acid residues (page 639, column 1 and 2). However, the reference does not explicitly teach the linking moiety that connects the biologically active compound and the transport moiety.

Noda, et al., teaches the bifunctional linking reagent S-acetylmercapto succinic anhydride (column 7, lines 40-59). The reagent is a general bifunctional linking reagent that acts as a spacer and can be used for linking two functionally distinct biologically active molecules.

It would have been obvious to one of ordinary skill in the art at the time invention was made to modify the method of splicing of the non-catalytic domain with the nuclear localization signal moiety as thought by Lorenzen, et al., and the use the bifunctional reagent to link the biologically active molecule with the transport moiety as taught by Noda, et al. One skilled in the art would have been motivated to link biologically active molecules to transport moiety for transporting molecules of interest into the cells. There would have been a reasonable expectation success given the fact that such conjugates can be synthesized and has been shown to have desired biological activity as shown by the aforementioned references. Therefore, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1654

Bruce Campell

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